

December 26, 1948.

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Dear Mike,

I have studied the manuscript as closely as I could, and after making a few minor alterations, am sending it on to the JEC.

Firstly, I want to apologize for a footnote "This is paper No. 389 in the journal series of the Department of Genetics" appended to my address. We have this rather arbitrary rule, and although I felt that this was primarily a California contribution, as would be indicated by the senior authorship, I was overruled about leaving it out. Fortunately, we no longer have to indicate "Approved by the Director of the Wis. Agr. Exp. Sta." on the paper, but I did have to go through the formality of securing approval.

It reads very well, and I think is an important contribution although Monod had anticipated the meat of it. Monod seems to be proceeding along lines very much like ours. I just had a letter from him in which he promised to send me a manuscript of some of his latest stuff, which I'll be glad to pass on. Perhaps fortunately, he has not had to worry about the complexity of the non-accumulation of glucose by the intact cells because he has been working types like K-12 rather than W-327.

The only changes that I have indicated are as follows:

p. 21. line five. strain has as yet been made,....

I put: "the absence of this enzyme cannot entirely account for the difference, etc." As it stood, I think there was the suggestion that the block in glucose utilization by W-108 as well as by W-327 was not in hexokinase function, which I don't think is what you have in mind so much as that this supposition, while possibly correct, is inadequate to account for the behavior of the intact cells. For the same reasons, I altered the first 2 words of p. 22, line 7 from "Another possible" to "An alternative" explanation,...

p. 23 line 14. I generalized the concept of semipermeability by inserting a parenthesis (or at other interfaces within the cell) after the word cell surface.

p. 24 line 4 "utilized" for "oxidised"

Also, I have rewritten the final paragraph, and the text description of the origin of the strains, in very trivial ways.

I hope that your reaction to these alterations is, at worst, neutral. I did not think that any of them violated your intentions, although I would certainly have sent them back to you for your study had you not indicated the desirability of promptness.

I am going to ask the journal to send me a separate order for reprints, as our accounting procedures are too involved to make it feasible to repay you for our part of a combined order.

I want to thank you very sincerely for your kind letter. I take it that you meant 1949 rather than 1948 as the summer when we might be able to make some arrangement to come out to Berkeley. I don't think I could handle your job; at any event, the main reason that I made that suggestion was in hopes of having an opportunity to work a little more closely with you, on your own home grounds, on these problems. For the same reason, please do not press any arrangements at Caltech.

As you pointed out, there are a number of questions still unsettled. I would like to hear whether you have any further plans. I am especially concerned to find out which enzymes are affected by which enzymes. Possibly, ~~phosphorylase~~ ~~phosphorylase~~ negative mutants can be detected (from Y-10) by the iodine reaction on colonies grown on maltose. Do you have any information on polysaccharide accumulation in intact cells? Also, I've received a small sample of isomaltose (glucose -6-glucoside) from Dr. E. Montgomery, and propose to test it as a substrate for W-327. I imagine that one of the first items in any further work would be the determination of hexokinase activity in W-108, Y-10 and W-327. Do you propose to do this?

The complete utilization of maltose by W-327 is certainly the least satisfactory hiatus in this last paper. Clearly, either maltose is altered prior to its reaction yielding polysaccharide, (eg. to maltose-1-phosphate) or glucose is produced from the reaction in a form different from that in which we can supply it. It might be possible to test this last supposition by assaying for "active" glucose with W-108. Glucose-1-phosphate is not available to K-12 for growth, probably due to penetration problems, so this compound would not interfere. This experiment is not likely to work, but it may be worthwhile.

Do you have any suggestions as to the relationship between the coli polysaccharide and amylose? Intact K-12 scarcely utilizes amylose, amylopectin, bacterial dextrans, or the bacteriological grade commercial dextrans, but this may, too, be a permeability problem.

Sincerely,

  
Joshua Lederberg